Eur J Vasc Endovasc Surg 33, 717–724 (2007)
doi:10.1016/j.ejvs.2006.12.012, available online at http://www.sciencedirect.com on ScienceDirect

Late Outcome of Spinal Cord Stimulation for Unreconstructable and Limb-threatening Lower Limb Ischemia

P.A. Gersbach,[1*] V. Argitis,[1] J.-P. Gardaz,[3] L.K. von Segesser[1] and E. Haesler[2]

Departments of [1]Cardiovascular Surgery, [2]Angiology, and [3]Anesthesiology, University Hospital (CHUV), 1011 Lausanne, Switzerland

Objectives. *To determine whether the initial benefits of spinal cord stimulation (SCS) treatment for critical limb ischemia (CLI) persist over years.*
Design. *Analysis of data prospectively collected for every CLI patient receiving permanent SCS. Follow-up range 12 to 98 months (mean 46 ± 23, median 50 months).*
Population. *87 patients (28% stage III, 72%stage IV) with unreconstructable CLI due (83%) or not (17%) to atherosclerosis and with an initial sitting/supine transcutaneous pO2 gradient >15 mmHg.*
Methods. *Assessment of actuarial patient survival (**PS**), limb salvage (**LS**) and amputation-free patient survival (**AFPS**). Analysis of the impact of 15 risk factors on long-term outcomes using the Fischer's exact test for categorical variables and the t test for continuous variables.*
Results. *Follow-up was complete for patient and limb survival. A single non-atherosclerotic patient died during follow-up. Among atherosclerotic patients **PS** decreased from 88% at 1y, to 76% at 3y, 64% at 5y and 57% at 7y. **LS** reached 84% at 1y, 78% at 2y, 75% at 3y and remained stable thereafter. Diabetes was found to affect **LS** ($p < 0.05$) and heart disease to reduce **PS** ($p < 0.01$). **AFPS** was reduced in heart patients ($p < 0.01$), diabetics ($p < 0.05$) and in patients with previous stroke ($p < 0.05$).*
Conclusions. *In CLI patients the beneficial effects of SCS persist far beyond the first year of treatment and major amputation becomes infrequent after the second year.*

Keywords: Spinal cord stimulation; Critical limb ischemia; Long-term outcomes; Risk factors; Microcirculatory screening.

Introduction

Beneficial effects of spinal cord stimulation (**SCS**) on both ischemic pain and microcirculatory blood flow have long been demonstrated.[1–5] In contrast, the influence of SCS on limb salvage in patients with critical limb ischemia (**CLI**) has been constant matter of debate. Several investigators[7–11] have found that the long-term outcome of SCS treatment is closely related with the preprocedural condition of the microcirculation. SCS cannot be expected to reopen mechanically occluded microvessels albeit it can reduce the microcirculatory spastic changes from CLI.[3,4] Among the multiple tests available to differentiate between occlusive and spastic microcirculatory changes the variation of tcpO2 in the supine and sitting position has emerged as a simple and reliable test.[7–9] A recent meta-analysis of controlled trials matching 444 patients concluded to significantly higher limb salvage at 12 months with SCS than with conservative treatment.[6] As for a large majority of surgical vascular studies, however, these reports unfortunately focus on limb salvage and quality of life at 12 months. As a consequence accurate long-term data on limb salvage (**LS**) in SCS patients are still lacking.

This study aims to review our ongoing SCS experience with follow-up extending up to 9 years, to assess treatment durability, long-term limb and patient survival, and to investigate which factors may influence these outcomes.

Methods

This clinical trial was conducted in a specialist vascular unit at a university teaching hospital. The

*Corresponding author. P.A. Gersbach, MD, Centre Hospitalier Universitaire Vaudois, Department of Cardiovascular Surgery, Rue du Bugnon 46, CH-1011 Lausanne, Switzerland.
E-mail address: philippe.gersbach@chuv.ch

1078–5884/000717 + 08 $32.00/0

demographic characteristics of the patients, degree of ischemia, previous vascular treatments, co-morbidities, implantation procedures as well as outcome at discharge and during the follow-up period were prospectively introduced into a database. All data entered in the database before the end of May 2005 were reviewed and analyzed. Limb salvage was defined as preservation of the heel and of the walking capacity of the patient.

Patients with limb ischemia due to atherosclerosis and those with non-atherosclerotic peripheral arterial occlusive disease (**PAOD**) were distributed into 2 different groups and evaluated separately.

Patients selection and routines

Our policy is to reserve SCS treatment to the few patients who are in a stable and severely symptomatic Fontaine's stage III or IV[12] and who don't have ischemic ulcers larger than 4 centimeters. These patients must have been deemed both unreconstructable and medically intractable by a consensus multidisciplinary decision involving angiologists, interventional radiologists and vascular surgeons; moreover, they must be free of major cognitive deficits and have a minimal life expectancy of one year.

Noninvasive tests are routinely used to confirm the arterial origin of the symptoms. Atherosclerotic patients with ankle and toe pressure not indicative of category 4 or 5 of the Rutherford's classification are excluded.[13] The transcutaneous oxygen partial pressure (**tcpO2**) is measured at the dorsum of the forefoot in the supine and sitting positions. Patients with a supine tcpO2 over 35 mmHg, which corresponds to the lower limit (30–50 mmHg) of the TransAtlantic Inter-Society Consensus for diagnosing CLI,[14] and those with a positional tcpO2 difference (ΔtcpO2) <15 mmHg[7] are discarded. Exceptions were made in this study in 2 patients with previous controlateral amputation and in 4 cases in which the skin conditions could not guarantee accurate tcpO2 measurements.

A single experienced surgeon is responsible for all implantations. Postoperative standard controls are systematically performed in the outpatient vascular unit after 3 weeks, 3 months 6 months, 1 year, and on an annual basis thereafter. These controls include an interview focusing on pain, comfort, quality of life (**QOL**), degree of satisfaction and intercurrent disease. A physical examination, tcpO2 measurements in the supine and sitting position and technical controls of the stimulation system are repeated at each control. Persistent acral lesions are treated by an independent orthopedic surgeon who freely decides whether and at which level an amputation has to be performed. Amputations at any level above the heel are considered major.

Preparation and surgical technique

Electrodes are exclusively implanted in patients with an INR <1.2 and a partial thromboplastin time (PTT) <35 seconds. Subcutaneous heparin is discontinued 12 hours and intravenous heparin 4 hours preoperatively. Antiplatelet agents are stopped 7–10 days before the planned intervention. Electrodes are always implanted under local anesthesia and intravenous antibiotics (intravenous amoxicillin/clavulanic acid 1.2 g ttd for 48 hours or a single preoperative shoot of 1 g Vancomycin). The epidural space is entered with a Tuohy needle usually at the middle lumbal level and a quadripolar electrode is placed under fluoroscopic guidance at the Th 9-Th 10 level. Stimulation is begun and the electrode is manipulated until the patient reports comfortable paresthesias in the whole aching area. The electrode is then fixed to the thoracolumbal fascia and connected to a percutaneous extension cable linked to a portable external stimulating device. Subcutaneous implantation of an internal impulse generator is proposed after 5 to 12 days of trial stimulation to patients presenting both a substantial reduction of pain symptoms and a measurable tcpO2 increase in the supine position.

Risk factors

The impact of 15 factors on both long-term major amputation and patient survival in atherosclerotic patients was assessed. They were: Age, gender, Fontaine stage III vs lV, preoperative supine tcpO2, diabetes, hypertension, chronic renal failure, chronic obstructive pulmonary disease (COPD), heart disease requiring chronic specific treatment, atrial fibrillation, previous stroke or transient ischemic attack (TIA), controlateral amputation, previous sympathectomy, previous thrombolysis and previous prostaglandine treatment. Diseases present in less than 10% (such as persistent smocking, cancer or HIV infection) were considered too rare for statistical evaluation.

Statistical analysis

The main outcomes of interest were patient survival, limb survival and amputation-free patient survival. Survival times were calculated from the date of electrode implantation to the date of death or of major limb amputation. The Kaplan-Maier curves presented

at Figs. 1–3 were established with the aid of the statistical package for the Social Science (SPSS version 8.0, Chicago IL, USA). The influence of various risk factors on the long-term outcome was assessed by the Fisher's exact test for categorical variables and by the Student t test for continuous variables; all tests were bidirectional and p values <0.05 were considered statistically significant. A stepwise regression analysis was performed to predict the effect of confounding variables on event-free survival. The statistical package used for this analysis was JMP (Version 5.0, SAS Institute, Cary NC).

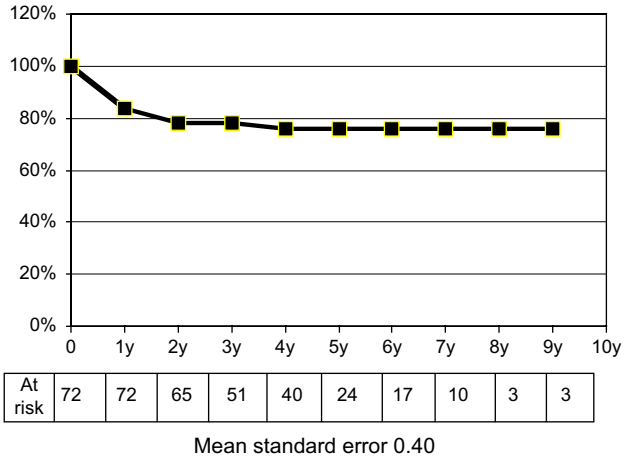

Fig. 2. Actuarial limb survival.

Results

A total of 87 consecutive patients received permanent SCS for otherwise intractable critical limb ischemia (**CLI**). All were in Fontaine's stage III or IV due to severe atherosclerosis in 72 (83%) and to non-atherosclerotic peripheral vascular disease in 15 (17%). For the whole series, follow-up was complete for patients and limb survival. It ranged from 1–9 years (mean 46 ± 23, median 50 months).

Of these 87 CLI patients 28% were in stage III and 72% in stage IV of the Fontaine's classification. The demographic and clinical baseline data of atherosclerotic and non-atherosclerotic patients are shown in Table 1.

Neither death nor neurological complication occurred within 30 days of surgery.

a) Non-atherosclerotic group. Non-atherosclerotic CLI of the lower extremities was mostly due to Buerger (8 patients) and to Raynaud (5 patients) diseases, and to complex regional pain syndrome (CRPS) and homocysteinemia in the remaining 2 cases. Previous treatment consisted in prostaglandin therapy in five patients and in sympathectomy in two.

Patients in the non-atherosclerotic group were significantly younger than atherosclerotic patients. After 3 weeks of SCS treatment all had substantially less pain and an improved microcirculation in the diseased area. Neither previous sympathectomy nor previous prostaglandins treatment influenced this outcome. The local tcpO2 value measured after 2–3 weeks of SCS in the supine position was used to guide amputations and excisions of necrotic tissue whenever necessary. All amputations were limited to the forefoot.

Survival in this small subgroup reached 93%. A women implanted at the age of 82 years retained her leg until her death from cardiac failure 4 years later. There was no other fatality in this group.

In 5 patient a stimulation intensity over 4.5 volts and in 2 others a pulse width over 700 milliseconds

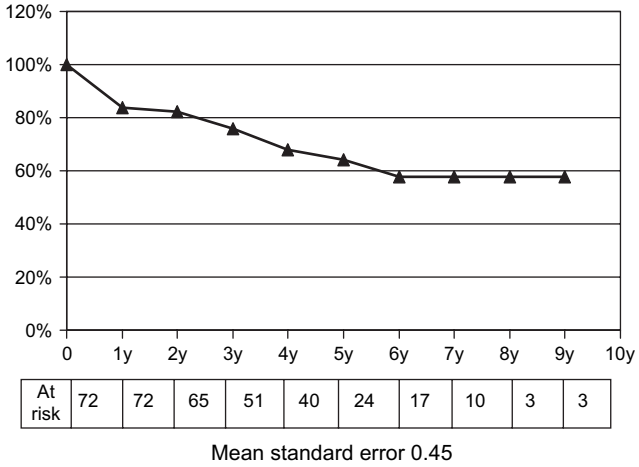

Fig. 1. Actuarial patient survival.

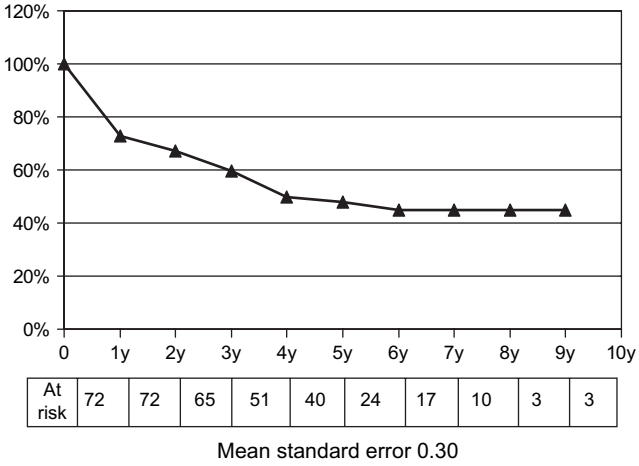

Fig. 3. Actuarial amputations-free patient survival.

Table 1. Baseline data of 87 patients

Parameter	Atherosclerotic PVD ($n=72$)	Non-atherosclerotic PVD ($n=15$)
Stage III/IV	19/53	5/10
Gender F vs M	27/45	4/11
Age mean	mean 75.5 ± 7.9 years*	mean 52.3 ± 17.7*
range	49–90 y.	32–82y.
median	76 y.	48y.
Follow-up	mean 47 ± 23 months	Mean 38 ± 22 months

*$p < 0.01$.

was required to cover the whole aching area. Such values were never applied in the atherosclerotic group.

Five re- interventions (29%) were necessary in 3 patients: 1 of them underwent two normal battery replacements and its electrode had to be changed because of severe epidural fibrosis; another patient had his battery replaced after 34 months; the third one, a Buerger patient, became symptom-free after 8 months and remained so until his battery became exhausted. After a period of observation we opted for the withdrawal of the whole system, and the patient has remained free of symptom for the last 13 months.

b) Atherosclerotic group. The main characteristics of most patients in this group are an advanced age (Table 1) and a poor general condition, as evidenced by the co-morbidities listed in Table 2.

Moreover, atherosclerotic patients were all referred to SCS at the very end-stage of the disease, with symptoms that would have absolutely required vascular reconstruction if feasible, and after multiple conventional conservative and invasive treatments had failed. Only 15 patients (21%) received SCS as a first operative treatment. Table 3 details the treatments attempted before SCS initiation.

Diasbling rest pain was present in all patients and skin ulcers of proven arterial origin were found in 3/4 of cases (stage IV). Infection along with lymphangitis and/or positive blood cultures was present in 21 patients. All received intravenous antibiotics for several days before electrode placement was considered feasible.

Table 2. Preoperative morbidity in atherosclerotic patients

Morbid condition	Nb	%	Comments
Diabetes	28	39%	19 × under insulin
Hypertension	42	58%	
Cardiopathy	36	50%	previous heart surgery in 22
Atrial fibrillation	18	25%	
Stroke/TIA	15	21%	permanent deficit in 7
Controlateral.amputation	7	10%	above knee in 2
Chronic renal insufficiency	16	22%	dialysis in 6
COPD	10	14%	
Varia	13	18%	9 carcinomas, 3 liver cirrhoses, 1 HIV

Table 3. Previous vascular treatments in atherosclerotic patients

Type of treatment	Number	
Only non-invasive treatments	15	(21%)
Surgery/angioplasty	0–10/patient	(mean 2.08)
Sympathectomy	16	(22.%)
Prostaglandines	15	(21%)
Thrombolysis	16	(22%)

Patient survival (PS), limb survival (LS) and amputation-free patient survival (AFPS) are presented in Figs. 1–3.

Nineteen patients (26%) died after a mean period of SCS treatment of 2.0 ± 1.6 years (median 21 months) due to heart failure ($n=12$), cancer ($n=4$), renal failure ($n=2$) and stroke ($n=1$). None of these deaths was attributable to immediate or delayed complications of SCS. Neither the gender nor the age at implantation did significantly influence mortality (Table 4). Mean age at the time of death was 79 ± 9.2 years.

Fifteen patients (21%) required a major amputation during the observation period. Among them 11 were amputated within 6 months of SCS treatment accounting for an early amputation rate of 15%. These early amputations were motivated by the recurrence of intractable pain at rest in 3 cases and by rapidly progressing tissue necrosis or infection in the other 8. Neither the incidence nor the time to major amputation was influenced by the Fontaine's stage at initial presentation.

Table 4. Influence of possible risk factors on SCS outcome in atherosclerotic patients

Risk factor	Amputation-free patient survival	Amputation	Death
Age	0.270	0.086	0.053
Gender	1.000	1.000	1.000
Stage III vs IV	0.180	0.183	0.763
Supine tcpO2	0.729	0.282	0.814
Diabetes	*0.023*	*0.011*	0.788
Hypertension	0.155	0.556	0.175
Heart disease	*0.0019*	0.209	*0.0010*
Atrial fibrillation	0.793	0.482	0.218
Stroke/TIA	*0.0213*	0.097	0.107
Renal failure	0.256	0.258	0.749
COPD	0.739	1.000	1.000
Controlat amput.	1.000	1.000	1.000
Sympathectomy	0.410	1.000	0.207
Prostaglandines	0.259	0.736	0.324
Thrombolysis	1.000	0.442	0.267

Stepwise regression analysis of amputation-free survival found a probability of adverse late event of 15.2% for heart disease, of 19.6% for heart disease and diabetes and of 22.5% for patients presenting with heart disease, diabetes an a previous stroke.

The influence of demographic and clinical risk factors on death, amputation and amputation-free patient survival is reported in Table 4.

The preoperative tcpO2 values in the whole atherosclerotic group ranged from 0 to 35 mmHg in the supine position (mean 11 ± 11.7 mmHg, median 6.5 mmHg) and from 7 to 69 mmHg in the sitting position (mean 36 ± 17.3, median 34.5 mmHg), allowing to calculate a mean supine/sitting preoperative tcpO2 gradient of 24.3 ± 12.1 mmHg (median 24 mmHg). Systematic tcpO2 controls at 3 ± 1 months in all amputation-free survivors evidenced a substantial tcpO2 increase in 46, minimal changes in 2 and deterioration in 4. Table 5 compares the mean values registered before and after 3 months of SCS in these 52 patients.

Major tcpO2 changes were infrequent beyond the third month of treatment. The mean value obtained at the last control in 40 amputations-free long-term survivors was 35.5 ± 16 mmHg (median 40) and 54.8 ± 14.7 mmHg (median 54) in the supine and sitting positions.

Forty-seven long-term survivors had no or very occasional pain at rest. Three of the 4 patients with decreased tcpO2 at 3 months and 2 patients with increased values still complained from severe resting pain. Among them 2 were amputated and 2 died shortly thereafter. The last patient decided to stay under morphinic agents until his death several months later. The ambulation capacity of most SCS responders was in correct adequation with their needs and remained so beyond the third month of treatment. No patient complained from ischemic pain during home activities; pain probably due to claudication arose after 100 to 400 meters in most patients and after 1 kilometer or more in 10%.

Thirty re-interventions were required over time (42%). Half of them consisted in normal battery replacement. Unexpected revision occurred in 21% because of electrode displacement (10 cases) or rupture (3 cases), premature battery depletion (1 case) and infection (1 case). Single revision procedures were performed in 22 patients and multiple procedures in 3. Only two patients required multiple electrode and/or cable revisions; of note both were amputees.

Table 5. Effects of 3 months of SCS treatment on tcpO2 values in 52 atherosclerotic amputations-free survivors

Position	Initial tcpO2 (mmHg)	tcpO2 at 3 months (mmHg)	Mean tcpO2 increase (mmHg)
supine	12.5 ± 11.6*** median 9	33.3 ± 17.1*** median 39	20.8 ± 14.8 median 22
sitting	40.6 ± 15.0*** median 40	56.7 ± 11.8*** median 58	16.1 ± 16 median 15.5

***$p < 0.001$, 2-tailed t-test.

Discussion

This first systematic study of the long-term effects of SCS on inoperable limb-threatening ischemia shows that the benefits on limb salvage commonly observed after 6 to 12 months of treatment[2,6,7,11,15,18,19] persist over time.

Selection of patients and planned follow-up controls are prerequisite to achieve the best treatment effect. Vascular specialists who applied tight preestablished microcirculatory criteria selected all patients. Hence, the results presented here cannot be compared with those reported by neurosurgeons anesthesiologists and pain specialists.

Current evidence indicates that the beneficial effects of SCS on limb ischemia are mostly mediated by early changes in the microcirculation.[3,4,9,16,17] Therefore only targeted microcirculatory tests are adequate to select potential treatment responders; tcpO2 measurements have emerged as the most simple and reliable test to achieve this goal.[7,9] A recent review of studies using tcpO2 to select SCS candidates has concluded that a strong selection based on a combination of tcpO2 measurements substantially improves limb salvage of CLI patients treated by SCS. On balance, however, the authors also estimated that such a stringent selection nearly halves the group of eligible patients.[18]

SCS is a particularly attractive option to treat non-atherosclerotic CLI because in such cases lesions are usually diffuse and located in the very distal part of the arterial system, where reconstruction is not feasible. In fact the subjective and objective results in the 15 non-atherosclerotic patients of this series were superior to those obtained in atherosclerotic cases. However, this series is definitely too small to allow any accurate conclusion. From a technical point of view the rather young age of most non-atherosclerotic CLI patients along with the often over average stimulation intensities required to cover the whole aching area make these patients good candidates for the newly available, albeit more expansive re-loadable batteries.

The outcome of patients receiving SCS for PAOD due to atherosclerosis is quite different. The mortality is high, but still less than reported in most PAOD studies.[20–22] This difference is attributable to the selection procedure that excludes the patients with a poor life expectancy as well as those with rapidly progressive ischemic necrosis, wet gangrene or

irreversible microcirculatory lesions. Importantly, however, the long-term non-survivors who could retain a functional leg until the end of their life still greatly benefited from SCS treatment.

Unexpectedly, SCS did not perform significantly better in stage III than in stage IV patients, most probably because the selection procedure tends to exclude patients with the worse microcirculatory condition.

When feasible, SCS appears definitely superior to conservative treatment in terms of mid and long-term limb survival. A recent review of 20 publications including over 6000 CLI patients found an over 70% limb amputation rate within 1 year among those treated conservatively.[22] This value contrasts strongly with the around 80% one-year limb survival obtained by SCS in both the present and other recent studies.[6,7,10,15,23] Less benefit, however, was found in SCS trials having not used microcirculatory selection criteria,[24–27] probably because these studies have included patients with irreversible microcirculatory lesions and, hence, no tissue healing potential.

After 1, 3 and 5 years of SCS limb salvage was similar to that of infrainguinal reconstructions[28,29] and the number of re-interventions was comparable to that of large vascular surgical series.[30,31] However both techniques cannot be compared, especially because SCS was never meant to be an alternative technique to reconstructive procedures, even in the very few patients who could have benefit from both techniques. Furthermore, reports on reconstructive procedures include a variable proportion of Fontaine's stage ll patients in which SCS has no proven benefit as well as a large number of patients in the most severe stage of the disease, who are beyond SCS treatment capabilities.

In the long run the functional results of SCS are certainly inferior to those of successful reconstructive procedures. Several studies[32–34] have pointed out the importance of functional outcomes measures after lower extremity revascularization. However, it was also found that instruments to measure these outcomes are difficult to administer to an elderly population because of the complexity of the rating scales, and because many questions in standard questionnaires do not pertain to the activities of older adults.[35] Indeed no firm data could be gained in this study on walking distances because most patients were unable to perform treadmill tests. The Walking Impairment Questionnaire[36] was considered inappropriate in the presence of multiple confounding factors such as severe musculo-skeletal, heart and lung diseases. Nevertheless, most of these rather aged and sedentary SCS responders declared themselves satisfied with a walking distance of several hundred meters. These patients compare favorably with the 46% of patients who are still nonambulatory 17 months after a below-knee amputation.[37] Notable decrease over time of the walking capacity was only observed in the few patients who finally required a late amputation and in almost every case of system dysfunction. Severe rest pain commonly recurred at the time of battery depletion, or of accidental system dysfunction; it always disappeared shortly after correction of the failure. This observation confirms that clinical improvement is due to SCS, and that the delivery of an adequate electrical current at the right spinal level is essential to keep its pain relieving effect.

Several experimental and clinical studies have concluded to a beneficial effect of SCS on the microcirculation of ischemic and non-ischemic tissues.[1,3,8,26,38] In the present study, after having increased during roughly 3 months, the tcpO2 values remained at the same stable level over time in the large majority of patients who did not require a late amputation. This stable enhancement of tcpO2 over time strongly suggests that lasting microcirculatory changes are responsible for the long-term benefits reported by most treatment responders. However, tcpO2 measurements being notoriously influenced by uncertain changes occurring in the heart and lung functions as well as in the texture of the skin and subcutaneous tissue, comparisons between tcpO2 values gained at wide intervals cannot be considered absolutely conclusive.

The necessity of re-interventions over time is a well-known major drawback of SCS treatment. In the present study re-interventions were more frequent than in other SCS trials.[19,39,40] This difference is mostly attributable to normal battery replacements that account for half of the re-interventions. Most of these re-interventions were performed after periods of time that are largely beyond the scope of trials with a shorter follow-up. These re-interventions had minimal consequences on the patient's overall condition. There were only 2 late electrode displacements and one late rupture. All occurred in patients with a previous controlateral limb amputation. Because the frequent torsion movements occurring in the spine of amputees in their daily lives, especially during transfers, it seems advisable to use an open surgical technique to implant electrodes in such cases.

Limitations of the study

The main limitation of this study is inherent to the indications to SCS treatment: Randomization is impossible because SCS is exclusively proposed to patients in whom both invasive and conservative treatments have already failed.

Because the many confounding problems related to the older age of the patients -mostly social isolation, depression and worsening of co-existent diseases- it was not possible to reliably assess the impact of SCS treatment on QOL outcomes.

Finally this study has neither been designed to provide early and mid-term data nor to test SCS applicability in CLI. Accordingly only limited comparisons can be made with results obtained with other kinds of treatment.

In conclusion, the present study has shown that the initial benefits of SCS treatment persist over time. High rates of re-interventions were required to maintain the benefit of SCS. The systematic use of microcirculatory tests has allowed identifying the tiny proportion of patients who have a fair chance to benefit from SCS treatment at the mid- and long-terms. Therefore, SCS for clinical limb ischemia must be regarded a true vascular treatment that definitely requires the competence of a skilled vascular laboratory and of vascular specialists.

References

1 Augustinsson LE, Holm J, Carlsson CA, Jivegard L. Epidural electrical stimulation in severe ischemia. Evidence of pain relief, increased blood flow and a possible limb saving effect. *Ann Surg* 1985;**202**:104–111.

2 Galley D, Rettori R, Boccalon H, Medvedowsky A, Lefebvre JM, Sellier F *et al*. La stimulation électrique médullaire dans les artériopathies des membres inférieurs: une étude multicentrique chez 244 patients. *J Mal Vasc* 1992;**17**:208–213.

3 Jacobs MJ, Jörning PJ, Joshi SR, Kistlaar PJ. Epidural spinal cord electrical stimulation improves microvascular blood flow in severe limb ischemia. *Ann Surg* 1988;**207**:179–183.

4 Jacobs MJ, Jörning PJ, Beckers RC, Ubbink DT, van Kleef M, Slaaf DW. Foot salvage and improvement of microvascular blood flow as a result of epidural spinal cord electrical stimulation. *J Vasc Surg* 1990;**12**:354–360.

5 Nachbur B, Gersbach Ph, Hasdemir M. Spinal cord stimulation for unreconstructible chronic limb ischemia (invited review article). *Eur J Vasc Surg* 1994;**8**:383–388.

6 Ubbink DT, Vermeulen H, Spincemaille GHJJ, Gersbach Ph, Berg P, Amann W. Systematic review and meta-analysis of controlled trials assessing spinal cord stimulation for inoperable critical limb ischemia. *Br J Surg* 2004;**91**:948–955.

7 Gersbach Ph, Hasdemir MG, Stevens RD, Nachbur B, Mahler F. Discriminative microcirculatory screening of patients with refractory limb ischemia for dorsal column stimulation. *Eur J Vasc Endovasc Surg* 1997;**13**:464–471.

8 Gersbach Ph. Microcirculatory screening for spinal cord stimulation. *Critical Ischemia* 1999;**9**(2):39–45.

9 Sciaccia V, Mingoli A, di Marzo L, Fiume CMD, Cavallaro A. Predictive value of transcutaneous oxygen tension measurements in the indication for spinal cord stimulation in patients with peripheral vascular disease: preliminary results. *Vasc Surg* 1989;**23**:128–132.

10 Amann W, Berg P, Gersbach Ph, Gamain J, Raphael JH, Ubbink DT for the SCS-EPOS Study Group. Spinal cord stimulation in the treatment of non-reconstructable stable critical leg ischemia: results of the European peripheral vascular disease outcome study (SCS-EPOS). *Eur J Vasc Endovasc Surg* 2003;**26**: 280–286.

11 Spincemaille GHJJ. Spinal cord stimulation in critical limb ischemia. Thesis, Maastricht 2001.

12 Fontaine R, Kim M, Kieny R. Die chirurgische Behandlung der peripheren Durch-blutungsstoerungen. *Helv Chir Acta* 1954; **21**:499.

13 Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S *et al*. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg* 1997;**26**: 517–538.

14 TransAtlantic Inter-Society Consensus (TASC). Management of peripheral arterial disease: Section D: chronic critical limb ischemia. *Eur J Vasc Endovasc Surg* 2000;**19**(Suppl. A):S144–S243.

15 Horsch S, Claeys L. Epidural spinal cord stimulation in the treatment of severe peripheral arterial occlusive disease. *Ann Vasc Surg* 1994;**8**:468–474.

16 Stanton-Hicks M, Salamon J. Stimulation of the central and peripheral nervous system for the control of pain. *J Clin Neurophysiol* 1997;**14**:46–62.

17 Claeys LGY. Improvement of microcirculatory blood flow under epidural spinal cord stimulation in patients with nonreconstructible peripheral arterial occlusive disease. *Artif Organs* 1997;**2**:201–206.

18 Ubbink DT, Gersbach Ph, Berg P, Amann W, Gamain J. The best TcpO2 parameters to predict the efficacy of spinal cord stimulation to improve limb salvage in patients with inoperable critical leg ischemia. *Int Angiol* 2003;**22**(4):356–363.

19 Ubbink DT, Vermeulen H. Spinal cord stimulation for non-reconstructible chronic critical leg ischemia (Cochrane review). *The Cochrane Library* (issue 3). Oxford: Update Software; 2003.

20 Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ *et al*. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med* 1992;**326**:381–385.

21 McKenna M, Wolfson S, Kuller L. The ratio of ankle and arm arterial pressure as an independent predictor of mortality. *Atherosclerosis* 1991;**87**:119–128.

22 Wolfe JHN, Wyatt MG. Critical and subcritical ischaemia. *Eur J Vasc Endovasc Surg* 1997;**13**:578–582.

23 Ubbink DT, Spincemaille GH, Prins MH, Reneman MS, Jacobs MJ. Microcirculatory investigations to determine the effect of spinal cord stimulation for critical leg ischemia: the Dutch multicenter randomized controlled trial. *J Vasc Surg* 1999;**30**:236–244.

24 Suy R, Gybels J, van Damme H, van Maele R, Delaporte C. Spinal cord stimulation for ischemic rest pain. The Belgian randomized study. In: Horsch S, Claeys L, eds. *Spinal cord stimulation: An innovative Method in the Treatment of PVD.* Steinkopf Verlag Darmstadt; 1994:197–202.

25 Jivegard LE, Augustinsson LE, Holm J, Risberg B, Örtenwall P. Effects of spinal cord stimulation (SCS) with inoperable severe lower limb ischaemia: a prospective randomised controlled study. *Eur J Vasc Endovasc Surg* 1995;**9**:421–425.

26 Claeys LG, Horsch S. Transcutaneous oxygen pressure as predictive parameter for ulcer healing in endstage vascular patients treated with spinal cord stimulation. *Int Angiol* 1996; **15**:344–349.

27 Klomp HM, Spincemaille GH, Steyerberg EW, Habbema JD, van Hurk H. Spinal cord stimulation in critical limb ischaemia; a randomized trial. ESES Study Group. *Lancet* 1999;**353**:1040–1044.

28 Leng GC, Davis M, Baker D. Bypass surgery for chronic lower limb ischaemia. *Cochrane Database Syst Rev* 2000;**3**:CD002000.

29 Al-Omran M, Tu JV, Johnston KW, Mamdani MM, Kucey DS. Outcome of revascularization procedures for peripheral arterial occlusive disease in Ontario between 1991 and 1998: a population-based study. *J Vasc Surg* 2003;**38**:279–288.

30 Nicoloff AD, Taylor LM, McLafferty MB, Moneta GL, Porter JM. Patient recovery after infrainguinal bypass grafting for limb salvage. *J Vasc Surg* 1998;**27**:256–266.

31 Pomposelli FB, Kansal N, Hamdan AD, Belfield A, Sheahan M, Campbell DR *et al*. A decade of experience with dorsalis pedis artery bypass; analysis of outcome in more than 1000 cases. *J Vasc Surg* 2003;**37**:307–315.

32 Landry GJ, Moneta GL, Taylor LM, Edwards JM, Yeager RA. Comparison of procedural outcomes after lower extremity reversed vein grafting and secondary surgical revision. *J Vasc Surg* 2003;**38**:22–28.
33 Thompson MM, Sayers RD, Reid A, Underwood MJ, Bell PR. Quality of life following infragenicular bypass and limb amputation. *Eur J Vasc Endovasc Surg* 1995;**9**:310–313.
34 Pomposelli Jr FB, Arora S, Gibbons GW, Frykberg R, Smakowski P, Campbell DR *et al*. Lower extremity arterial reconstruction in the very elderly: successful outcome preserves not only the limb but also residential status and ambulatory function. *J Vasc Surg* 1998; **28**:215–225.
35 Seabrook GR. Discussion of the publication by Nicoloff and associates. *J Vasc Surg* 1998;**27**:266.
36 Regensteiner JG, Steiner JF, Panzer RJ, Hiatt WR. Evaluation of walking impairment by questionnaire in patients with peripheral arterial disesase. *J Vasc Med Biol* 1990;**2**:142–152.
37 Nehler MR, Coll JR, Hiatt WR, Regensteiner JG, Schnickel GT, Klenke WA *et al*. Functional outcome in a contemporary series of major lower extremity amputations. *J Vasc Surg* 2003;**38**:7–14.
38 Linderoth B. Spinal cord stimulation in ischemia and ischemic pain. Possible mechanisms of action. In: Horsch S, Claeys L, eds. *Spinal Cord Stimulation ll*. Darmstadt: Steinkopf Verlag; 1995:19–35.
39 Mullet KR, Rise MT, Shatin D. Design and function of spinal cord stimulators- theoretical and developmental considerations. *Pain Digest* 1992;**1**:281–287.
40 Spincemaille GH, Klomp HM, Steyerberg EW, van Hurk H, Habbema JDF, for the ESES Study Group. Technical data and complications of spinal cord stimulation: data from a randomized trial on critical limb ischemia. *Stereotact Funct Neurosurg* 2000;**74**:63–72.

Accepted 13 December 2006
Available online 12 February 2007